



THE ROCKEFELLER UNIVERSITY

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PRESIDENT

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Dear Dr. Pinching:

You must have had many communications about your group's extraordinarily interesting paper on the association of Gc with AIDS as published in The Lancet for May 2.

The association, if anything is so sharp as to raise further questions about the possibility of different kinds of artifact. In your sample you can account for 30% of AIDS with the rare Gc 1f homozygote; but in San Francisco certainly a very much larger fraction of the total homosexual population is already infected: so much fewer than 30% of them can be 1f. There remains the likelihood that Gc is influencing the progression from serotype-positive to clinical disease -- a matter that I am sure you are investigating very diligently! Of course all of these numbers could be very readily reconciled if the Gc effect is to accelerate the manifestation of AIDS; and your London population may be temporally closer to its initiation than is the case in San Francisco (and the African later).

I did have to raise one unlikely alternative, but one that probably should be checked out explicitly: that the Gc 1f phenotype that you find in such strikingly large numbers among AIDS patients is a phenocopy, namely that something in the AIDS disease process itself is resulting in the misclassification of Gc 1f. One could spin various hypotheses to account for such a possibility but the easiest thing is to test it very directly. To belabor the obvious, you could look at some sample of your "1f homozygotes" among AIDS patients, to determine if their uninfected immediate relatives show an appropriate distribution of the 1f marker. You have such a strong association that even a handful of kindreds should be enough to corroborate that the Gc 1f marker in AIDS patients is an uncomplicated

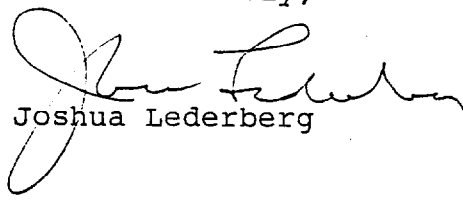
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legacy of inheritance of Gc 1f from their (almost always) heterozygous parents. This can be tested either directly in parents, or in a very reasonable way by the distribution of Gc 1f among their siblings.

In this country I am urging that very careful consideration be given to Gc screening in connection with the various other epidemiological studies that are being proposed.

Yours sincerely,



Joshua Lederberg